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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/812,862	03/20/2001	Jack R. Wands	00786-282003	2989

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EXAMINER
VOGEL, NANCY T

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/23/2003 / o

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/812,862	WANDS ET AL.	
	Examiner	Art Unit	
	Nancy Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37.CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7 and 8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claims 1-18 are pending in the case. Receipt of Drawings (8/27/01) Sequence listing (8/27/01), Information Disclosure Statements (3/20/01 and 2/1/02), and Change of Address (12/23/02) is acknowledged.

Claim Rejections - 35 USC § 112

Claims 1-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids encoding polypeptides as shown in Figure. 1 and which reduce replication of a hepadnavirus in vitro, does not reasonably provide enablement for all nucleic acids encoding polypeptides having any 70 amino acids of wild type hepadnavirus core protein which do not have this activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to a nucleic acid encoding a mutant hepadnavirus polypeptide, comprising at least 70 amino acids of a core protein, and having a deletion of 3-9 carboxyterminal amino acids (claims 1, 2), and a mutant hepadnavirus comprising said core protein fused to at least a portion of a hepadnavirus surface protein (claims 3-5), and a mutant hepadnavirus comprising at least 70 amino acids of a core protein fused to at least a portion of a surface protein (claim 6). There is no functional limitation in the claims. Applicants have taught that several mutant hepadnavirus core proteins, including several which are fused to portions of a hepadnavirus surface protein, reduce replication of a wild type hepadnavirus in vitro, and propose a dominant interfering mechanism.

The claims encompass an unreasonable number of inoperative polypeptides, which the skilled artisan would not know how to use. As opposed to the claims, what is disclosed about the hepadnavirus core protein's structure, and the mechanism of the reduction of replication seen with some of the mutant constructs, is minimal. The claims encompass mutants having any 70 amino acids of the core protein of any hepadnavirus, and the "comprising" language encompasses any insertions of any amino acids. There is no limitation requiring that the recited 70 amino acids be contiguous, and therefore the core protein could encompass virtually any 70 amino acids, so long as the terminal 3-9 (or more for claims 3-6) carboxyterminal amino acids of the wild type hepadnavirus core protein are deleted. The disclosed working examples include only core proteins whose aminoterminus is amino acid 1, and include contiguous amino acids to at least amino acid 171 for HBV (see Fig. 1). The state of the art at the time the invention was

made was not high, since it was not predictable which 70 amino acids of the HBV core protein would function to reduce replication of wild type hepadnavirus.

For these reasons, which include the complexity and unpredictability of the nature of the invention and art in terms of the mechanism of reduction of replication by mutants of the core protein, the limited working examples, the lack of direction or guidance for using polypeptides that are not identical to those mutants shown in Fig. 1, the breadth of the claims for structure without function, it would require undue experimentation to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 7, 8, 13, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Beams et al. (Virology 194:597-607 (1993) cited by applicant in IDS submitted 2/1/02).

Beams et al. disclose a nucleic acid encoding a polypeptide that comprises a first amino acid sequence of at least 70 amino acids in length that is identical to a region of a wild type HBV core protein and lacks a second amino acid sequence of the wild type HBV core protein, wherein the second sequence comprises the carboxyterminal three amino acids of the wild type HBV core protein and does not exceed nine amino acids in

length (see Fig. 1A, deletion of 7 carboxyterminal amino acids, designated Cd176). The reference discloses vectors containing said nucleic acid and cells containing said vectors (see page 600 first column line 17-28).

Claim 6, 12, and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Souw et al. (WO 94/12617).

Souw et al. disclose a nucleic acid encoding a polypeptide comprising a first amino acid sequence of at least 70 amino acids in length that is identical to a region of a wild type hepadnavirus core protein, and a second amino acid that is identical to a portion of a wild type hepadnavirus surface protein (see page 9, lines 25-33, page 21, line 25-34, page 41, line 7-36).

Claims 6, 12 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Rutter (US Pat. No. 4,859,465).

Rutter discloses a nucleic acid encoding a polypeptide comprising a first amino acid sequence of at least 70 amino acids in length that is identical to a region of a wild type hepadnavirus core protein, and a second amino acid that is identical to a portion of a wild type hepadnavirus surface protein, a vector comprising said nucleic acid, and host cells comprising said vector (see Example 1 and 2).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3-5, 9-11, 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Souw et al. (WO 94/12617) in view of Beams (Virology 194:597-607 (1993) (cited by applicant)).

Souw et al. disclose nucleic acids encoding polypeptides that comprise a first amino acid sequence of at least 70 amino acids in length that is identical to a region of a wild type hepadnavirus core protein, including one variant, delta 8, that has a deletion near the carboxyterminal end of the wild type hepadnavirus core protein, and which comprise an amino acid sequence that is identical to a portion of a wild type hepadnavirus surface protein, vectors containing said nucleic acids, and cells containing said nucleic acids (see abstract and page 21 lines 3-24).

The reference does not disclose said nucleic acid in which the first amino acid mentioned above has a deletion of at least the three carboxyterminal amino acids.

Beams et al. disclose a nucleic acid encoding a polypeptide that comprises a first amino acid sequence of at least 70 amino acids in length that is identical to a region of a wild type HBV core protein and lacks a second amino acid sequence of the wild type HBV core protein, wherein the second sequence comprises the carboxyterminal three amino acids of the wild type HBV core protein and does not exceed nine amino acids in length (see Fig. 1A, deletion of 7 carboxyterminal amino acids, designated Cd176). The reference discloses vectors containing said nucleic acid and cells containing said vectors (see page 600 first column line 17-28).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the nucleic acid disclosed by Souw et al. to include as the core protein element, the deletion mutants disclosed by Beames et al. having deletions of at least the carboxyterminal three amino acids, in the disclosed fusion protein, and to further include the nucleic acid in a vector, and in a cultured cell, since Souw et al. disclose that any hepadnavirus (e.g. HBV) core protein variant, including fragments thereof, in the disclosed fusion proteins.

One would have been motivated to include carboxyterminal deletions of the HBV core protein in the fusion proteins disclosed by Beams by the desire to express HBV antigens for the prevention or treatment of hepatitis or other undesirable consequences of HBV infection. The general teaching of any fragment or deletion of HBV core protein fused to a HBV surface protein is disclosed in the Souw et al. reference, and therefore was well known in the art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy Vogel whose telephone number is (703) 308-4548. The examiner can normally be reached on 7:30 - 4:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

ntv
9/12/03

TERRY MCKELVEY
PRIMARY EXAMINER